Mapping molecular landmarks of human skeletal ontogeny and pluripotent stem cell-derived articular chondrocytes.

Journal: Nat Commun

Publication Year: 2018

Authors: Gabriel B Ferguson, Ben Van Handel, Maxwell Bay, Petko Fiziev, Tonis Org, Siyoung Lee, Ruzanna Shkhyan, Nicholas W Banks, Mila Scheinberg, Ling Wu, Biagio Saitta, Joseph Elphingstone, A Noelle Larson, Scott M Riester, April D Pyle, Nicholas M Bernthal, Hanna Ka Mikkola, Jason Ernst, Andre J van Wijnen, Michael Bonaguidi, Denis Evseenko

PubMed link: 30194383

Funding Grants: Promoting survival and countering hypertrophy of pluripotent stem cell (PSC)-derived chondrocytes, Promoting survival and countering hypertrophy of pluripotent stem cell (PSC)-derived chondrocytes, Pluripotent stem cell-derived chondrocytes for articular cartilage repair

Public Summary:
Tissue-specific gene expression defines cellular identity and function, but knowledge of early human development is limited, hampering application of cell-based therapies. Here we profiled 5 distinct cell types at a single fetal stage, as well as chondrocytes at 4 stages in vivo and 2 stages during in vitro differentiation. Network analysis delineated five tissue-specific gene modules; these modules and chromatin state analysis defined broad similarities in gene expression during cartilage specification and maturation in vitro and in vivo, including early expression and progressive silencing of muscle- and bone-specific genes. Finally, ontogenetic analysis of freshly isolated and pluripotent stem cell-derived articular chondrocytes identified that integrin alpha 4 defines 2 subsets of functionally and molecularly distinct chondrocytes characterized by their gene expression, osteochondral potential in vitro and proliferative signature in vivo. These analyses provide new insight into human musculoskeletal development and provide an essential comparative resource for disease modeling and regenerative medicine.

Scientific Abstract:
Tissue-specific gene expression defines cellular identity and function, but knowledge of early human development is limited, hampering application of cell-based therapies. Here we profiled 5 distinct cell types at a single fetal stage, as well as chondrocytes at 4 stages in vivo and 2 stages during in vitro differentiation. Network analysis delineated five tissue-specific gene modules; these modules and chromatin state analysis defined broad similarities in gene expression during cartilage specification and maturation in vitro and in vivo, including early expression and progressive silencing of muscle- and bone-specific genes. Finally, ontogenetic analysis of freshly isolated and pluripotent stem cell-derived articular chondrocytes identified that integrin alpha 4 defines 2 subsets of functionally and molecularly distinct chondrocytes characterized by their gene expression, osteochondral potential in vitro and proliferative signature in vivo. These analyses provide new insight into human musculoskeletal development and provide an essential comparative resource for disease modeling and regenerative medicine.